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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,621	02/15/2006	Judy Lieberman	033393-055184	1751

7590  
David S Resnick  
Nixon Peabody  
100 Summer Street  
Boston, MA 02110

08/04/2008

EXAMINER
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PITRAK, JENNIFER S

ART UNIT	PAPER NUMBER
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1635

MAIL DATE	DELIVERY MODE
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08/04/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/533,621	<b>Applicant(s)</b> LIEBERMAN ET AL.	
	<b>Examiner</b> JENNIFER PITRAK	<b>Art Unit</b> 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 01 May 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 62-70 is/are pending in the application.
- 4a) Of the above claim(s) 68 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 62-67 and 69-70 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>02/08/2008</u> .  | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

### *Remarks*

In the amendments file 05/01/2008, Applicants canceled claims 71-76 and amended claim 62.

Claim 68 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 09/20/07.

Claims 62-67 and 69-70, insofar as they relate to elected SEQ ID NOs:1 and 2, are currently being examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The Declaration of Judy Lieberman, Premrata Shankar, Sang-Kyung Lee, Erwei Song, and Manjunath Narasimhaswamy under 37 C.F.R. 1.131 regarding the "Beresford" reference, filed 05/01/2008, has been considered and is accepted.

The Declaration of Judy Lieberman, Premrata Shankar, and Sang-Kyung Lee under 37 C.F.R. 1.131 regarding the "Novina" reference, filed 05/01/2008, has been considered, but is not accepted for the reasons set forth below.

### ***Claim Rejections - 35 USC § 112 - WITHDRAWN***

The amendments to the claims have obviated the rejection of claims 62-67 and 69-70 under 35 USC § 112, first paragraph.

***Claim Rejections - 35 USC § 102 - WITHDRAWN***

The rejection of claims 62, 63, 67, 69, and 70 under 35 U.S.C. 102(e) as being anticipated by Beresford, *et al.* (US 2004/0248296, of record) is withdrawn in view of the Declaration of Judy Lieberman, Premlata Shankar, Sang-Kyung Lee, Erwei Song, and Manjunath Narasimhaswamy under 37 C.F.R. 1.131, filed 05/01/2008.

***Claim Rejections - 35 USC § 103 - MAINTAINED***

Claims 62, 63, 65, 67, 69, and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takaku, *et al.* (1999, JP11-292795, of record) and Novina, *et al.* (2002, Nat. Med. v.8:681-686, of record). This rejection is maintained for the reasons of record.

**Response to Arguments**

Applicants argue that the rejection under 35 U.S.C. § 103(a) should be withdrawn because the references do not serve as anticipatory prior art under 35 U.S.C. § 102. This argument is not persuasive because the rejection is under 35 U.S.C. § 103(a). Furthermore, Applicants' argument that the Declaration filed 05/01/2008 sets forth that Lieberman, Shankar and Lee, Novina, Murray, Dykxhoorn, Beresford, Riles, and Sharp did not contribute to conception of the claimed invention is not persuasive because the Declaration does not show that the reference invention (the "Novina" reference) is not by "another". According to the MPEP 706.02(b), a rejection based on 35 U.S.C. 102(a) can be overcome by filing an affidavit or declaration under 37 CFR 1.132 showing that the *reference invention* (emphasis added) is not by "another." The "Novina" reference has a 102(a) date, and as such can be overcome by such an

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affidavit or declaration. The Declaration filed on 05/01/2008 does not establish that the authors of the Novina reference did not contribute to the Novina reference. In fact, to the contrary, the Declaration clearly establishes that all of the authors contributed to the Novina reference. The Declaration states that "While Novina D.D., Murray M. F, Dykxhoorn D.M., Beresford, P.J., Riles, J., and Sharp, P. are properly credited to purposes of the Novina publication," (item 4 on the Declaration of J. Lieberman, P. Shankar, and S. Lee).

***Claim Rejections - 35 USC § 103 - NEW***

Claims 62-67, 69, and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takaku, *et al.* (1999, JP11-292795, of record), Wissenbach (U.S. PGPub 2003/0125241, filed as provisional application 60/291,830 on 05/18/2001), Bass (2001, Nature, v.411:428-9), Elbashir, *et al.* (2001, Nature, v.411:494-8) (Elbashir 1), and Elbashir, *et al.* (2001, EMBO J., v.20:6877-88) (of record, 01/22/2008 IDS) (Elbashir 2).

The claims are to a method for treating a viral infection comprising administering to an individual an siRNA having sense sequence, SEQ ID NO: 1, and antisense sequence, SEQ ID NO: 2.

Takaku, *et al.* teach methods of HIV infection prophylaxis using antisense oligonucleotides directed against CCR5. Takaku, *et al.* claim HIV cofactor inhibitors that contain oligonucleotides complementary to the CCR5 gene and that the claimed inhibitors can be used for prophylaxis against HIV infection and/or for HIV infection therapy (Claim 1 and beginning of "Detailed Description of the Invention"). Specifically, Takaku, *et al.* teach the antisense oligonucleotide comprising SEQ ID NO: 47 (Figure 1), which is complementary to the

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mouse CCR5 gene sequence from position 855 to position 874. Takaku, *et al.* further teach that such therapeutic oligonucleotides can be formulated with liposomes and can be administered orally, parenterally, or locally and in the form of lotions, ointments, and suppositories (paragraph [0029]). Takaku, *et al.* do not teach the use of siRNAs to treat or prevent HIV infection, nor do they specifically teach topical or intravaginal administration. Takaku, *et al.* also do not teach siRNAs having SEQ ID NO: 1 and SEQ ID NO: 2. They do not teach siRNAs targeting the HIV p24 gene.

Wissenbach, *et al.* teach the use of siRNAs for prevention and therapy against HIV infection (p.2, paragraph 10; p.4, paragraph 38; p.18, paragraph 154; p.21, paragraph 197). Specifically, Wissenbach teach targeting CCR5 and p24 (p.7, Table 2; p.9, paragraph 85).

It was well known at the time of filing of the instant application that siRNAs were extremely useful for "knocking down" gene expression by RNA interference (RNAi). Bass teaches that RNA interference, mediated by double-stranded small interfering RNAs (siRNAs), was very well-recognized as a very useful tool for studying gene function once the sequence of a gene is known, that RNAi was accessible to all scientists, and that RNAi is now routine in laboratories (p.428, first paragraph). Elbashir 1 teaches that siRNA duplexes provide a new tool for studying gene function in mammalian cells, and that siRNAs may eventually be used as gene-specific therapeutics (abstract and last paragraph).

Elbashir 2 also teaches that already in 2001, RNAi had rapidly developed into an important tool for reverse genetics and had been shown to be useful in mammalian cells if the siRNAs are less than 30 base-pairs in length (p.6878, second paragraph). They report their systematic analysis of length, overhangs, and sequence determinants of siRNA function. They

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conclude their report with guidelines for designing efficient siRNAs for inhibiting target gene expression (p.6855, “The siRNA user guide”). Elbashir, *et al.* describe efficient siRNAs as those duplexes composed of 21-nt sense and 21-nt antisense RNAs that form a 19-bp double helix with 2-nt 3'-overhanging ends. The authors further explain that target recognition is highly sequence-specific and is mediated by the siRNA complementary to the target, the 3'-most nucleotide of the guide siRNA does not contribute to the specificity of target recognition, while the penultimate nucleotide of the 3'-overhang affects target RNA cleavage and a mismatch reduces RNAi 2- to 4-fold, and that the 5'-end of the guide siRNA can have more mismatches to the target RNA when compared with the 3'-end. The authors further explain that nucleotides in the center of the siRNA are important for siRNA specificity determinants, the relative orientation of the siRNA duplex in the endonuclease complex determines the strand that can be used for target recognition, and give recommendations for the types and sequences of the 3'-overhanging sequences to ensure that the desired siRNA strand is the mRNA targeting strand. The authors describe that asymmetry in the siRNA-endonuclease complex or the target site sequence or accessibility of the target RNA may cause variation in efficiency of siRNA activity. Elbashir, *et al.* clearly demonstrate variation in siRNA efficiency for target inhibition and set forth guidelines for the design of siRNAs. On page 6886, in their concluding remarks, Elbashir, *et al.* indicate that their results are important for the design of efficient siRNAs for silencing genes in *Drosophila melanogaster* and they provide a basis for similar studies in other organisms.

It would have been obvious to one of ordinary skill in the art at the time of the instant application to target the CCR5 gene, as taught by Takaku, et al., with siRNAs, as taught by Wissenbach et al., for the treatment of HIV infection. It further would have been obvious to

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target the p24 gene in combination with CCR5, given the teachings of Wissenbach, et al. that both genes are appropriate HIV targets for nucleic acid-based therapy. It would have been obvious to make siRNAs with the instantly claimed SEQ ID NOs because Bass and Elbashir (1 and 2) make it clear that production of any siRNA sequence, including the instantly claimed SEQ ID NO: 1 and SEQ ID NO: 2, would be a matter of routine experimentation and optimization, as Elbashir 2 set forth siRNA design guidelines. It further would have been obvious to treat HIV infection by topically or intravaginally administering liposomal formulations of CCR5-targeting siRNAs because Takara *et al.* teach local delivery of the antisense formulations, which include lotions and ointments, which are topical formulations, and formulations that also include suppositories, which are intravaginal formulations. Based on Takara, et al.'s teaching of antisense-targeting of CCR5, one would have had a reasonable expectation that siRNA-targeting of CCR5 would effectively treat HIV infection. Thus, the claims as a whole would have been obvious to one skilled in the art at the time of the instant application.

### ***Closing***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER PITRAK whose telephone number is (571)270-3061. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Pitrak  
Patent Examiner  
Art Unit 1635

/Tracy Vivlemore/  
Primary Examiner, Art Unit 1635